



संजय गॉधी स्नातकोत्तर आयुर्विज्ञान संस्थान, लखनऊ
SANJAY GANDHI POST GRADUATE INSTITUTE OF MEDICAL SCIENCES,
Raebareli Road, Lucknow- 226014 (India)

Dr. Vinita Agrawal
Professor (Pathology) and
Member Secretary, Institutional Ethics Committee

Communication of decisions of the 107th Institutional Ethics Committee

IEC code: 2018-207-EMP-107

PGI/BE/344/2018

Agenda Item No. 16

Date: 09-May-19

Title of project: Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of Pharmacological intervention to improve sleep on these parameter

Principal Investigator: Dr U C Ghosal

Department: Gastroenterology

Name and Address of Institution: Sanjay Gandhi Postgraduate Institute of Medical Sciences,
Raebareli Road, Lucknow, 226014

New/Re-review project: New

Date, time and venue of meeting: 19-Jan-19 11.00 AM at Committee room of Guest house SGPGI

Dear Dr.

Institutional Ethics Committee reviewed and discussed your application to conduct the research study during the IEC meeting held on 19-Jan-19

List of documents reviewed:

1. Project Submission Form
2. Study Protocol
3. Case Report Form
4. Consent of Head of the PI's Department
5. Research Committee/Department committee /Doctoral Committee/Scientific Committee Approval
6. Undertaking by the PI
7. Conflict of Interest Statement by PI
8. CV of investigator outside SGPGI or of the student
9. Participant Information document (PID) consent forms CF) in English and Hindi



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The following members of the Institutional Ethics committee (IEC) were present at the meeting held on 19-Jan-19

Dr Chandishwar Nath Retd Chief Scientist CSIR-CDRI Lucknow - Chairman (Officiating)

Prof S.K Misra, Dean SGPGI - Member

Justice Vishnu Sahai Former Chief Justice Allahabad High Court - Member

Shri Vijai Varma, Chairman Upbhokta Forum Lucknow - Member

Shri Sharat Pradhan Senior Journalist Lucknow - Member

Prof Manish Kumar Verma Deptt of Sociology BBAU, Lucknow - Member

Dr. Mohan Gurjar, Deptt. Of CCM, SGPGI, Lucknow - Member

Prof. Vinita Agrawal, Deptt. Of Pathology, SGPGI, Lucknow - Member Secretary

IEC has taken following decisions for the study/trial;

Scientific issues, ethical issues and PID, CF were discussed.

The committee has given the following suggestions to the PI:

1. If the drug 'Melatonin' is indicated and approved for therapy, what is the beneficial outcome of this study?
2. Justify the use of placebo?
3. Mention the side-effects of the drug. Mention the provision of support and medical treatment for study related adverse side-effects.
4. The study involves 'evaluation of sleep abnormalities'. Include a psychiatrist in the study.
5. Mention source of healthy controls.
6. Mention method of randomization.
7. The study will require CTRI registration before start of study.
8. Submit properly framed separate PID's for controls, patients and legally accepted relative (LAR). Mention the collection of blood and stool also in the PID.
9. The departmental research committee meeting on 2/1/2019, however, the meeting minutes



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signed on 30/12/2018. Clarify.

Decision Major Modification. Kindly resubmit revised protocol and other documents.

PI advised to submit above correction within 4 weeks, failing which the project will not be considered in next IEC meeting for ethical approval.

As per above recommendations of IEC, the project/trial with documents has been placed for the reviewed by the following 3 - members committee.

1. Dr. Chandishwar Nath, Member Scientist G and Chief Scientist, Division of Toxicology, CDRI, Lucknow
2. Dr. Vinita Das Dept. of Obst. And Gynae, KGMU, Lucknow
3. Dr. Vinita Agrawal, Prof, Dept of Pathology, SGPGIMS, Lucknow

The 3- members has gone through the required documents suggested by IEC and following decision has been taken,

'Decision:Approved.'

The approval is valid until one year or duration of project whichever is later from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of annual status report.

Following points must be noted:

1. IEC should be informed of the date of commencement of study (AN5-V2/SGSOP 06/V3) and annual progress.
2. PI and other investigators should co-operate with IEC, which may monitor the trial from time to time.
3. The decision was arrived at through consensus. Neither PI nor any of proposed study team members was present during the decision making of the IEC.
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD and getting IEC concurrence and submitting status report, including accounts details should be submitted to HOD, IEC and extramural sponsors.
5. The IEC functions in accordance with the GCP-CDSCO/ICMR/Schedule Y guidelines/ICH-GCP.



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6. New information or any SAE, which could affect any study, must be communicated to IEC and sponsors. The PI should report SAEs occurred for IEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the Bioethics cell should receive the SAE reporting form within 24 hours of the occurrence.

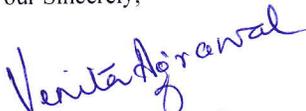
7. In the events of any protocol amendments, IEC must be informed and the amendments should be highlighted in clear terms

8. Any deviation/violation/waiver in the protocol must be informed to the IEC as detailed in AN1-V3/SGSOP 09/V3.

9. If project/drug/device trial initiation not done in next 6 months from date of approval from IEC, further extension will not be granted and it will require resubmission to IEC.

We hereby confirm that the Institutional Ethics Committee is organized and operates as per amended schedule Y (20th Jan 2005), ICH GCP guidelines and applicable regulations.

Thanking You,
Your Sincerely,


(Dr. Vinita Agrawal)

Member Secretary

IEC, SGPGI, Lucknow.

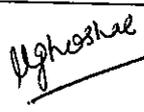
AN1-V1/SGSOP 03/V1

Project Submission Form for Review by IEC (6 copies and a CD required)

A. Identification details:

<p>*IEC Code No. (To be filled by the Bioethics cell):</p>
<p>Study/Protocol No. (For drug/device trials/any other, to be filled by PI):</p>
<p>Type of project: Intramural [<input type="checkbox"/>] Extramural [<input checked="" type="checkbox"/>] Drug trial/device [<input type="checkbox"/>] Independent [<input checked="" type="checkbox"/>] MD/DM/MCh/PhD/SRF Project [<input type="checkbox"/>] Collaborative [<input type="checkbox"/>] Other [<input checked="" type="checkbox"/>]</p>
<p>Status of review: New [<input checked="" type="checkbox"/>] Revised [<input type="checkbox"/>]</p>
<p>Proposal Title: Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters</p>

B. Investigator details:

	Name, Designation, Qualifications	Departmental Tel Nos. & Email ID	Signature
**PI	Dr Uday Chand Ghoshal, DM Professor Gastroenterology SGPGI	CUG:8004904780 Ext (O) 4405 (R) 4406 Email: udayghoshal@gmail.com	
1.Co-PI	Dr Ujjala Ghoshal, Professor, Microbiology SGPGI	CUG:8004904513 Ext(O) 5221 (R) 4406 Email: ujjalaghoshal@yahoo.co.in	

****One page recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience for new or investigator outside SGPGI or of the student (MD/MS/DM/MCh/PhD) who has submitted thesis/project**

C. Sponsor Information: Applicable [✓]

Not applicable []

1. **Name of sponsor/CRO:** Will be submitted to UP CST for funding after Ethics clearance

2. **Indian:** a) **Government** Central State Institutional
 b) **Private**

3. **International:** **Government** Private UN Agencies

4. **Industry:** National Multinational

5. **Contact address of sponsor/CRO:** Not applicable

6. **Budget: Rs.** Provided in the project

7. **Details of allocation of budget in Clinical Trial Agreement:** Yes [] No [] Not applicable

D. Study related Information:

1. **Design of study:** Epidemiological Basic Sciences Behavioral
 Clinical Interventional Single Centre Multicentre

2. No. of participants:	SGPGI	Total (if multicentre)
Patient*	97	97
Control*	97	97

3. **Duration of study:** Two years

4. **Duration of subject participation (no. of visit by a participant in study):** Two
**Please mention sample size calculation and source of control in methodology*

The related case-control studies were reviewed for calculation of sample size. The frequency of sleep disorder among IBS was observed to be 35% and 43% whereas in control it has been observed to be 29 and 14% respectively. Taking the average of these, we considered among IBS case and controls the average frequency of sleep disorder is 40% and 22%, respectively, considering a power of 80%, alpha value of 0.05 and ratio of case to control is 1:1. As per the

calculation, we propose to include 97 cases and 97 controls.

For interventional study with melatonin and placebo, sample size was calculated based on the data that improvement occurred in 88% patients if treated with melatonin as compared to 47% with placebo (Lu WZ. APT 2005; 22: 927-934). Hence, 34 patients will be treated with melatonin and 34 with placebo (two sided CI 99%, power 80%, case:control 1:1, and p value <0.05).

Considering 20-25% loss to follow-up, 97 patients with IBS will be randomized to melatonin and placebo.

E. Interventional study: Yes [] No [] **If No, move to next section i.e.**

NA

1. Does the study involve use of Drugs <input checked="" type="checkbox"/> Devices <input type="checkbox"/> Vaccines <input type="checkbox"/> Radiopharmaceutical <input type="checkbox"/> Recombinant DNA/Gene therapy <input type="checkbox"/> Stem cell <input type="checkbox"/> (need BARC approval) (need DBT- GEAC approval (NAC-SCRT registration and approval) Indian Systems of Medicines/ Alternate systems of Medicine <input type="checkbox"/> Any Other <input type="checkbox"/> None <input type="checkbox"/>	
2. Is it approved and marketed In India <input checked="" type="checkbox"/> UK & Europe <input checked="" type="checkbox"/> USA <input checked="" type="checkbox"/> Other Countries, Specify _____	
3. Does it involve a change in use, dosage, route of administration? Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> If yes, whether DCGI's/Any other Regulatory Authority's Permission is obtained? Yes <input type="checkbox"/> No <input type="checkbox"/> If yes, copy of permission attached. Yes <input type="checkbox"/> No <input type="checkbox"/>	
4. Is it an Investigational New Drug? Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> If yes a. Investigator's Brochure enclosed Yes <input type="checkbox"/> No <input type="checkbox"/> b. Preclinical studies data available (If yes, provide summary) Yes <input type="checkbox"/> No <input type="checkbox"/> c. Clinical studies data available (If yes, provide summary) Yes <input type="checkbox"/> No <input type="checkbox"/> d. Clinical study is Phase I <input type="checkbox"/> Phase II <input type="checkbox"/> Phase III <input type="checkbox"/> Phase IV <input type="checkbox"/> NA <input type="checkbox"/> If phase I-III will the drug/device be provided free? Yes <input type="checkbox"/> No <input type="checkbox"/> If phase IV will the drug/device be provided at cost less than Yes <input type="checkbox"/> No <input type="checkbox"/> Hospital pharmacy? e. DCGI's permission obtained Yes <input type="checkbox"/> No <input type="checkbox"/> If yes, copy of letter enclosed Yes <input type="checkbox"/> No <input type="checkbox"/>	
5. Data monitoring a. Is there a plan for reporting of adverse events? Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> If yes, reporting will be done to Sponsor <input type="checkbox"/> IEC <input checked="" type="checkbox"/> b. Is there a plan for interim analysis of data? Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>	
6. Provision for travel/treatment due to injury out of study Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>	

If yes, by Sponsor <input type="checkbox"/> Investigator <input checked="" type="checkbox"/> Insurance Company <input type="checkbox"/> Any Other <input type="checkbox"/> 7. Registered with Clinical Trial Registry – India Yes <input type="checkbox"/> No <input type="checkbox"/> If yes copy of certificate enclosed Will be done after Ethics clearance Yes <input type="checkbox"/> No <input type="checkbox"/>
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F. Details of participant of study:

1. Will subjects from both sexes be recruited: Yes [<input checked="" type="checkbox"/>]	No [<input type="checkbox"/>]
2. Inclusion/exclusion criteria given: Yes <input checked="" type="checkbox"/> []	No [<input type="checkbox"/>]
3. Type of subjects: Volunteers [<input checked="" type="checkbox"/>]	Patients [<input checked="" type="checkbox"/>]
4. Vulnerable subjects Yes [<input type="checkbox"/>]	No [<input checked="" type="checkbox"/>]
(if Yes tick the appropriate boxes)	
Pregnant Women [<input type="checkbox"/>]	Children [<input type="checkbox"/>] Elderly [<input type="checkbox"/>] Fetus [<input type="checkbox"/>]
Illiterate [<input type="checkbox"/>]	Handicapped [<input type="checkbox"/>] Terminally ill [<input type="checkbox"/>] Seriously ill [<input type="checkbox"/>]
Mentally challenged [<input type="checkbox"/>]	Economically & socially backward [<input type="checkbox"/>] Any other [<input type="checkbox"/>]
5. Special group subjects: Yes [<input type="checkbox"/>]	No [<input checked="" type="checkbox"/>]
(if Yes tick the appropriate boxes)	
Captives [<input type="checkbox"/>]	Institutionalized [<input type="checkbox"/>] Employees [<input type="checkbox"/>] Students [<input type="checkbox"/>]
Nurses/Dependent [<input type="checkbox"/>]	Staff [<input type="checkbox"/>] Armed Forces [<input type="checkbox"/>] Any Other [<input type="checkbox"/>]

G. Privacy and confidentiality:

1. Study Involves	Direct Identifiers (Pt. identified by name/Cr. no.) <input type="checkbox"/>
	Indirect Identifiers/Coded (Pt. identified after break of code) <input checked="" type="checkbox"/>
	Completely Anonymised /Delinked (Pt. cannot identified) <input type="checkbox"/>
2. Confidential handling of data by staff	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>

H. Detail of sample collection (If no sample being collected, move to next section i.e. I):

A. Regarding sample collection

1. Collection of organs or body fluids or blood. If yes, please specify Yes No

Type: ~~Blood~~, urine, stool

Amount each time 5ml Total 5 ml

No. of time two
urine

2. Collection of fetal tissue or abortus. If yes, please specify Yes No

3. Use of pre-existing/stored/left over samples. If yes, please specify Yes No

4. Proper disposal of material Yes No

B. Special situation

1. Will any sample collected from the patients be sent abroad? Yes No

If yes, give details and address of collaborators

a. Sample will be sent abroad because (Tick appropriate box)

- Facility not available in India
- Facility in India inaccessible
- Facility available but not being accessed

If so, reasons _____

b. Has necessary clearance been obtained Yes No

2. Collection for banking/future research Yes No

I.

Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters

Investigators

Uday C Ghoshal, Prof. Dept. of Gastroenterology, SGPGI, Lucknow

Ujjala Ghoshal, Prof. Dept. of Microbiology, SGPGI, Lucknow

Brief proposal summary:

Irritable bowel syndrome (IBS), a common gastrointestinal (GI) disorder in India and in the rest of the World, is enigmatic in its pathogenesis. IBS is associated with recurrent abdominal pain or discomfort, bloating, incomplete evacuation, altered bowel habit, and abnormal stool forms (1, 2). The etiology of IBS remains unclear and different factors were thought to be involved like, genetics and environmental factors, visceral hypersensitivity, altered gut microbiota or disorder of the microbiota-gut-brain axis and various psychological factors like anxiety, depression, and insomnia or sleep disturbance (3). Due to increasing work pressure in today's society, and the consequent shift duty and psychological stress, the frequency of sleep disorders is increasing; disturbed sleep may be associated with a vicious cycle in which altered sleep may result in gastrointestinal (GI) disturbances, which in turn, may jeopardize sleep further. Disorder of the gut microbiota, the largest organ of the human body, is being suggested to be responsible for several GI and extra-GI diseases. Qualitative change in gut microbiota is currently studied by next generation sequencing. Gut and sleep patterns work in an axis - a two-way street of communication, some studies reported altered gut microbiota or dysbiosis modulates peripheral

and central nervous system function, leading to alterations in brain signaling and behavior that possibly leads to sleep disturbances (4).

Several case control and meta-analyses have reported an association between sleep disturbance and irritable bowel syndrome (IBS) as compared to healthy controls. However, the data regarding relationship between sleep disturbance and severity parameters of IBS have not been widely reported; moreover, interventions that improve disturbed sleep on these parameters are scanty. There is no systematic study on sleep disorders among patients with IBS from India.

Melatonin is a hormone made by the pineal gland; its biosynthesis is initiated by the uptake of the essential amino acid tryptophan and is an important inducer of sleep. Abnormality in melatonin has been shown in several studies on patients of IBS and functional constipation. A few studies also reported improvement in sleep and GI function after administration of melatonin. However, these studies had limitations due to small sample size, lack of randomization and inclusion of patients without sleep disorder. Moreover, there is no study from India on this issue (5,6,7).

Accordingly, we wish to undertake a study with the following aims:

- (i) Quality of sleep among patients with IBS and healthy controls.
- (ii) Levels of 6-Hydroxymelatonin sulphate (metabolite of melatonin) both in patients with IBS and healthy controls.
- (iii) Relationship between the IBS symptom severity (IBS-SSS), Health-Related Quality of Life (HRQL) and sleep disorder and melatonin deficiency,
- (iv) Relationship between gut dysbiosis and the above parameters
- (v) Effect of melatonin administration on IBS symptoms, HRQL and sleep.

Since sleep disturbance may be an important issue in IBS, the patients with IBS will be treated both with melatonin and standard treatment. Parameters like IBS-SSS, HRQL (8), Hospital Anxiety and Depression Scale (HADS) score (9), Pittsburgh Sleep Quality Index (PSQI) (10) will be studied in patients with IBS and healthy controls and these parameters would be repeated after 1 and 3 months follow-up in patients only. Urinary 6-Hydroxymelatonin sulphate will be studied in patients and controls before treatment with melatonin and it will be repeated after one month among patients with IBS only. Sleep study will be performed by PSQI questionnaire and also by polysomnography depending on the availability of the instrument. Study will analyse the effect of melatonin in GI and sleep disorder functions. Data will be analyzed using appropriate statistical techniques. P-values lesser than 0.05 will be considered significant.

Study protocol:**Sample size:**

The related case-control studies were reviewed for calculation of sample size. The frequency of sleep disorder among IBS was observed to be 35% and 43% whereas in control it has been observed to be 29 and 14% respectively. Taking the average of these, we considered among IBS case and controls the average frequency of sleep disorder is 40% and 22%, respectively, considering a power of 80%, alpha value of 0.05 and ratio of case to control is 1:1. As per the calculation, we propose to include 97 cases and 97 controls.

For interventional study with melatonin and placebo, sample size was calculated based on the data that improvement occurred in 88% patients if treated with melatonin as compared to 47% with placebo (Lu WZ. APT 2005; 22: 927-934). Hence, 34 patients will be treated with melatonin and 34 with placebo (two sided CI 99%, power 80%, case:control 1:1, and p value

<0.05). Considering 20-25% loss to follow-up, 97 patients with IBS will be randomized to melatonin and placebo.

Inclusion criteria

- Diagnosis by ROME III/IV criteria.
- Willing to participate and informed consent is obtained.

Exclusion criteria

- Presence of alarm symptoms such as severe organic GI diseases, unexplained iron deficiency anaemia, unintentional weight loss, palpable abdominal mass.
- No active substance intake.

Fund Requirements:

Detailed year wise breakup under the heading of staff, Equipment, Contingencies etc. (List of the items/ compounds may be given)

Amount of grant proposed: (in Rs.)

		Ist year	IInd year	Total
Staff	Junior Research Assistant (JRA)	2,40,000	2,40,000	4,80,000
Contingencies		5,50,000	2,70,000	5,32,000
Equipments		Nil	Nil	Nil
Grand total		7,90,000	5,10,000	13,00,000

Contingencies:

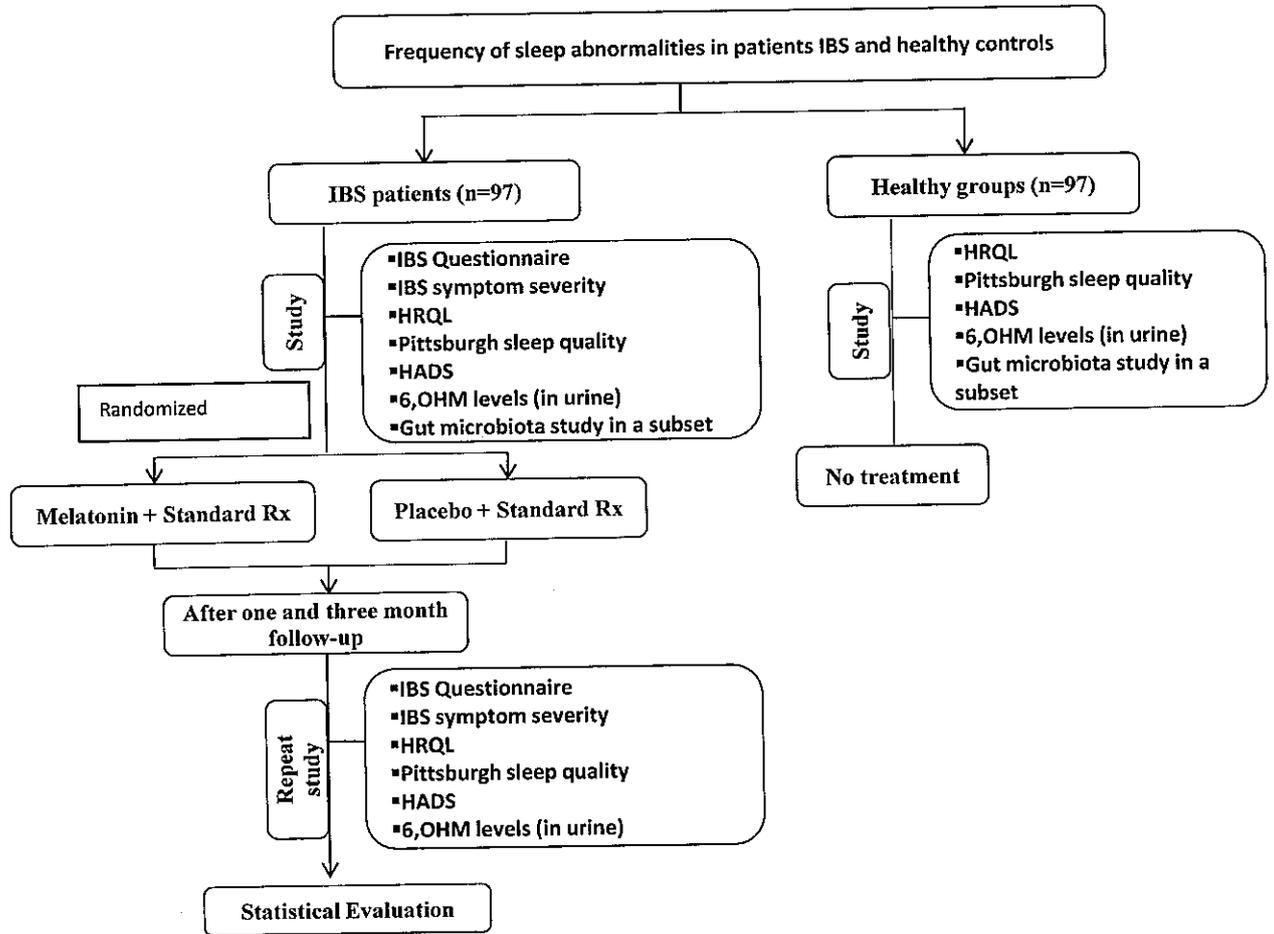
DNA extraction kits, Oligonucleotide primers, SYBR[®] Green master mix, Melatonin-Sulfate
Urine ELISA kit, other lab reagents and glassware, ladder, Agarose, Taq polymerase, dNTPs,
PCR tubes, Microtips, pipettes, gut microbiota next-generation sequencing.

References

1. Ghoshal UC, Shukla A. Malnutrition in inflammatory bowel disease patients in northern India: frequency and factors influencing its development.
2. Makharia GK, Ramakrishna BS, Abraham P, Choudhuri G, Misra SP, Ahuja V, Bhatia SJ, Bhasin DK, Dadhich S, Dhali GK, Desai DC. Survey of inflammatory bowel diseases in India. *Indian Journal of Gastroenterology*. 2012 Dec 1; 31(6):299-306.
3. Kinnucan JA, Rubin DT, Ali T. Sleep and inflammatory bowel disease: exploring the relationship between sleep disturbances and inflammation. *Gastroenterology & hepatology*. 2013 Nov;9(11):718.
4. De Palma G, Collins SM, Bercik P, Verdu EF. The microbiota-gut-brain axis in gastrointestinal disorders: stressed bugs, stressed brain or both? *The Journal of physiology*. 2014 Jul 15; 592(14):2989-97.
5. Mozaffari S, Abdollahi M. Melatonin, a promising supplement in inflammatory bowel disease: a comprehensive review of evidences. *Current pharmaceutical design*. 2011 Dec 1;17(38):4372-8.
6. Talero E, García-Mauriño S, Motilva V. Melatonin, autophagy and intestinal bowel disease. *Current pharmaceutical design*. 2014 Sep 1; 20(30):4816-27.
7. Siah KT, Wong RK, Ho KY. Melatonin for the treatment of irritable bowel syndrome. *World journal of gastroenterology: WJG*. 2014 Mar 14; 20(10):2492.
8. Ojeda C, Cofré C. Health related quality of life in pediatric patients with inflammatory bowel disease. *Revistachilena de pediatria*. 2018 Apr 1; 89(2):196-201.
9. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. *Actapsychiatrica Scandinavica* 1983; 67:361-370

10. Buysse DJ, Reynolds CF, 3rd, Monk TH, et al: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research* 1989; 28:193-213

Flowchart:



Brief proposal summary

Aim(s) and objectives, methodology describing the potential risks and benefits, outcome measures (maximum 500 words).

uCGwd

Signature of PI**Name:** Dr Uday Chand Ghoshal**Date:** 30/12/18

*** Please also submit detail **Study/Project Protocol** separately (Short review of literature, justification for study, aim, methodology, inclusion, exclusion criteria, statistical analysis).

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AN2-V1/SGSOP 03/V1

Consent of Head of the PI's Department

Date: 30.12.2018

I have reviewed the project "Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters" submitted by **Dr Uday C Ghoshal**, Principal Investigator from my department. I endorse the project and have 'no objection' for submission for consideration by Ethics committee.

I concur with the participants / investigators included in the study.

 Acting H. O. D. Dept. of Gastroenterology Signature & date LUCKNOW-226001 30/12/18	Professor & HOD	Gastroenterology
	Name	Department

AN3-V1/SGSOP 03/V1

Department research committee Approval

The project titled "Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters" with all the accompanying documents listed above was reviewed by the Research committee/department committee /doctoral committee/scientific committee presented on ----- at SGPGI. The committee has granted approval on the scientific content of the project. The proposal may now be reviewed by the Institutional Ethics Committee for granting ethical approval.

Abhishek
.....Signature of *HOD
Asst. Prof. of Gastroenterology
S.G.P.G.I.M.S.
LUCKNOW-226001
Date: 30/12/18

***In case of student (MD/MS/DM/MCh) or independent project/extramural**

****In case of intramural**

*****In case of PhD or any other project**

******Not applicable to sponsor/CRO initiated drug/device trials**

The PI should also attach a copy of minutes of "Research committee/department committee /doctoral committee/scientific committee".

AOP
30.12.18
Dr. Amit Goel
Assistant Professor
Department of Gastroenterology
SGPGIMS, Lucknow

Abhishek
30/12/18
Dr. Abhishek Kumar
Assistant Professor
Department of Gastroenterology
SGPGIMS, Lucknow

Vinod Kumar
30/12/18
Dr. Vinod Kumar MD, DM
Assistant Professor
Department of Gastroenterology
SGPGIMS, Lucknow

Gaurav
30/12/18
Dr. Gaurav Panda
Associate Professor
Dept. of Gastroenterology
SGPGIMS, Lucknow

UCCG
Dr. UDAY C GHOSHAL
M.D., D.N.B., D.M., F.A.C.G.
Department of Gastroenterology
SGPGI, Lucknow-226014

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AN4-V1/SGSOP 03/V1

Undertaking by the Principal Investigator

1. Name of the project:

Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters

2. Name, designation and department of the principal investigator:

Dr Uday Chand Ghoshal
Professor
Gastroenterology, SGPGI

3. Other members of the research team:

Dr Ujjala Ghoshal, Microbiology, SGPGI, Lucknow

4. Name and address of any other medical college, hospital or institution where parts of the study will be done:

5. Number of ongoing projects/clinical trials in which you are PI:

a. Number of clinical trials with active enrolments: 5

b. Number of clinical trials with follow up only: 0

c. Total number of ongoing projects/clinical trials (Projects+a+b): ...5....

1. I confirm that I will initiate the study only after obtaining all regulatory clearances.
2. I will not implement any deviation from the approved protocol without prior consent of the sponsor nature and it will be intimated to the IEC at the earliest.
3. I confirm that the Co-PI and other members of the study team have been informed about their obligations and are qualified to meet them.

4. I will personally supervise the study and ensure that requirements of obtaining informed consent and other ethical requirements under national regulatory and ICMR guidelines are adhered to.
5. I will maintain accurate and complete record of all cases in accordance with GCP provisions and make them available for audit/inspection by IEC, regulatory authorities, sponsors or their authorized representatives.
6. I will inform the IEC and the sponsors of any unexpected or serious adverse event at the earliest and definitely within seven days of its occurrence.
7. I will maintain confidentiality of the identity of all participating subjects and assure security and confidentiality of study data.
8. I and my colleagues will comply with statutory obligations, requirements and guidelines applicable to such clinical studies.
9. I will inform IEC if there is change in funding agency/status.
10. I will inform IEC of the date of starting the study within 2 weeks of initiation of the trial and submit annual progress reports and final report to Member Secretary, IEC within 4 weeks of the due date.

Dr Uday Chand Ghoshal

Signature of PI

Name_ Dr Uday Chand Ghoshal

Date_ 30.12.2018

Not applicable

CV* of PI or Investigator outside SGPGI or of the Student

Name:		
Date of Birth (dd/mm/yy):		Sex: Male [] Female []
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator):		
Professional Mailing Address: (Include institution name)		Study Sited Address: (Include institution name)
Telephone (Office):		Mobile Number:
Telephone (Residence):		E-Mail:
Academic Qualifications (Most current qualification first):		
Degree/Certificate	Year	Institution, Country
Current and Previous 3 Relevant Positions Including Academic Appointments (Most current position first):		
Month and Year	Title	Institution/Company, Country
Brief Summary of Relevant Clinical Research Experience:		
Signature:		Date:

*Signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience for new or investigator outside SGPGI or of the student (MD/MS/DM/MCh/PhD) who has submitted thesis/project

**Guidelines for Devising a Participant / Legally Acceptable Guardian
Information Document (PID) in English**

Kindly refer to Table 3.2 for the essential elements of an informed consent document. For example, of PID in non-interventional studies, see appendix (AP7/V3). For 'Recommended Terms for use in Informed Consent Document', see appendix (AP12/V3)

1. Study Title

Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters

2. Invitation Paragraph

You are being invited to take part in a research/trial study. Before you decide it is important for you to understand why the research/study is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your treating physician/family doctor if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. What is the purpose of the study?

The purpose of the study is to find out sleep abnormalities among patient with irritable bowel syndrome and control. Relationship of this sleep abnormality with all factors like:

- (i) Quality of sleep among patients with IBS and healthy controls.
- (ii) Levels of 6-Hydroxymelatonin sulphate (metabolite of melatonin) both in patients with IBS and healthy controls.
- (iii) Relationship between the IBS symptom severity (IBS-SSS), Health-Related Quality of Life (HRQL) and sleep disorder and melatonin deficiency,
- (iv) Relationship between gut dysbiosis and the above parameters
- (v) Effect of melatonin administration on IBS symptoms, HRQL and sleep.

Whether correcting the sleep abnormality by pharmacotherapy will lead to improvement of quality of life.

4. Why have I been chosen?

There will be two sheets available

1. Healthy volunteer sheet.
2. Patient sheet: You have been chosen because you have been suffering from IBS and do not meet any exclusion criteria namely:
 - Presence of alarm symptoms such as severe organic GI diseases, unexplained iron deficiency anaemia, unintentional weight loss, palpable abdominal mass.
 - Not proper informed consent.

- No active substance intake.

5. Do I have to take part?

It is entirely voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

6. What will happen to me if I take part?

If you take part you will be given some questionnaire which you have to fill up either yourself or if you have any difficulty a research assistant will help you to fill up. In addition a blood sample 5ml will withdraw and also you will ask to give urine and stool sample. In addition you may have to undergo a sleep study which involves connecting some machine to your body and you have to sleep one night while these machines are connected to. Subsequently, you will be allocated to treatment with a drug or placebo. Drug is melatonin and then you will have to undergo repeat test.

7. What do I have to do?

You have to fill up questionnaire, and you have to give sample of urine, stool, and blood. You have to do get a sleep study done and all this will be free of cost.

8. What is the drug or procedure that is being tested?

Effect of melatonin on your sleep, quality of life and hospital anxiety and depression scale is being studied.

9. What are the alternatives for diagnosis or treatment?

You will receive standard of care (in case of diarrhea-IBS: remosetron, constipation-IBS: Psyllium husk and, and plain-IBS: otilonium bromide and peppermint). However, you are also receiving melatonin and placebo. Alternative to melatonin is alprazolam, zolpidem and diazepam. They are not as safe sleeping medicine as melatonin.

10. What are the side effects of taking part?

Melatonin is a safe medicine. However, it can cause some side effects including headache, short-term feelings of depression, daytime sleepiness, dizziness, stomach cramps, and irritability.

11. What are the possible disadvantages and risks of taking part?

Melatonin is an approved drug is being used as a standard of care for patients with sleep dysfunction and as outlined above is quite free from side effects.

12. What are the possible benefits of taking part?

26

Data from this study will be used to optimize the management of IBS. This information can also be used for research for the community.

13. What if new information becomes available?

The information's collected from this study will be helpful in clinical management of IBS.

14. What happens when the research/trial study stops?

It will not affect your treatment. You will be continuously care for by the clinician as usual.

15. What if something goes wrong?

Though not much wrong is expected to occur, in case some problem arises, arrangement will be made to care for this we by the team caring for you including any specific treatment, as needed.

16. Will my taking part in this study be kept confidential?

All information collected about you during the course of the research/trial will be kept strictly confidential. Any information which leaves the hospital/clinic/laboratory will have your name and address removed so that you cannot be recognized from it. However, if needed Ethics committee may be allowed to see the records.

17. What will happen to the results of the research/trial study?

We will look in to the data at the end of the study and form results. Even if the data is published your personal information will not be disclosed in it.

18. Who is organizing and funding the research/trial?

The study is conducted by Department of Gastroenterology, SGPGI. The patients participating in the study will not pay anything for the study.

19. Will the drug be made available after trial is over? (new drug requires continued use, till it is marketed in India)

The drug is already approved and available in the market as standard of care

20. Who has reviewed the study?

IEC and departmental research committee have reviewed the study.

21. Contact for further information

If you had any further information about study or need to contact the study team at any time, you may contact the following:

Thank you for participating in the study.

UCC-101

Dr Uday Chand Ghoshal, DM
Professor
Gastroenterology
SGPGI
Ph:8004904780

Ext:4407

Name of the Member Secretary of Ethics Committee and address with telephone numbers.

The PID should be dated and given a version number. It should state that the participant will be given a copy of the information sheet and the signed consent form.

uCGm

Signature of PI

Name Uday C Ghoshal

Date 30.12.2018

Dr Vinita Agrawal
Member Secretary Ethics Committee.



AN8-V3/SGSOP 03/V3

Consent Form (English)

Study Title _____

Study Number _____

Subject's Full Name (with father's name) _____

Date of Birth/Age _____

Address of subject _____

Qualification _____

Occupation: Student/self-employed/service/housewife/other (please tick as appropriate)

Annual income of subjects _____

Name and address of nominee(s) and his relation to subject _____

1. I confirm that I have read and understood the information document dated _____ for the above study and have had the opportunity to ask questions.
OR I have been explained the nature of the study by the Investigator and had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/study, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study/ trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
5. I permit the use of stored sample (tissue/blood) for future research. Yes No
6. I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness _____

Received a signed copy of Participant Information Document and Consent Form.

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

_____ Date _____

AN13-V1/SGSOP 03/V1

**Checklist of Documents (6 copies and a CD of all documents listed below)
(Non Interventional trial require documents listed in Item no. 1 to 13)**

Please give page no. to all documents (start from 1, 2, 3.....40 and so on.)

**Please provide version no. and date of each document (for drug/device trial)*

Protocol Title: Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters
Principal Investigator: Dr Uday Chand Ghoshal, Professor, Gastroenterology, SGPGI
Type of document: Independent project

Item No.	Mandatory Documents (*with version and date)	Yes	No	NA	Page No.
1.	Document Receipt Form (to be submitted in duplicate, AN14-V1/SGSOP 03/V1)	✓			↓ 1-6
2.	Project Submission Form (AN1-V1/SGSOP 03/V1)	✓			9-17
3.	Study Protocol (Review of literature, aim, methodology, inclusion, exclusion criteria)	✓			18
4.	Case Report Form (form to capture data)				
5.	Consent of Head of the PI's Department (AN2-V1/SGSOP 03/V1)	✓			19
6.	Research committee/department committee /doctoral committee/scientific committee approval (AN3-V1/SGSOP 03/V1)	✓			20-21
7.	Undertaking by the PI (AN4-V1/SGSOP 03/V1)	✓			22
8.	Conflict of Interest Statement by PI (AN5-V1/SGSOP 03/V1)	✓			
9.	CV of new or investigator outside SGPGI or of the student (AN6-V1/SGSOP 03/V1)			NA	
10.	Participant Information document (PID) & consent forms CF) in English and Hindi (and if required in any other language) (AN 7to 10 -V1/SGSOP 03/V1) * Include guardian and parents				23-34
11.	Child Information Document and assent form in English and Hindi (and if required in any other			NA	

	language) (AN11-12-15V1/SGSOP 03/V1)				
12.	Ethics Committee clearance of other centers (in case of collaborative project)			NA	
13.	Clinical Trials Registry- India (CTRI) is a pre-requisite for clinical trials. In other case this must be done after approval by IEC				will be applied after ethics clearance
14.	Investigator Brochure			NA	
15.	Advertisement/Information brochure			NA	
16.	Insurance policy and certificate			NA	
17.	DCGI approval letter/DCGI submission letter			NA	
18.	NOC from DCGI /ICMR/DBT			NA	
19.	Director General of Foreign Trade (DGFT) approval in case study samples are to be sent abroad for analysis			NA	
20.	Genetic Engineering Advisory Committee (GEAC) approval in case study involves use of gene therapy/recombinant DNA			NA	
21.	Bhabha Atomic Research Centre (BARC) approval in case study involves use of radioisotopes/ionizing radiations			NA	
22.	Stem cell (NAC-SCRT registration and approval)			NA	
23.	DCGI marketing/manufacturing license for herbal formulations/nutraceuticals			NA	
24.	Clinical Trial Agreement (CTA)/Memorandum of Understanding (MOU)			NA	
25.	Material Transfer Agreement (MTA)- Health Ministry Screening Committee (HMSC) approval in case the study involves collaboration with any foreign laboratory/clinic/institution			NA	
26.	IEC processing fee (applicable for sponsored trials)			NA	
27.	Any other documents			-	

AN14-V1/SGSOP 03/V1

IEC Document Receipt Form (to be submitted in duplicate)

Type of Submission:	<input checked="" type="radio"/> New <input type="radio"/> Revised
Protocol Title: Frequency of sleep abnormalities in patients with irritable bowel syndrome and its relationship with symptom severity, quality of life and effect of pharmacological intervention to improve sleep on these parameters	
Principal Investigator: Dr Uday Chand Ghoshal, Professor, Gastroenterology, SGPGI	
Type of document: Independent project	

Checklist to assess the projects before they are submitted to IEC review

Item No.	Mandatory Documents (*with version and date)	Yes	No	NA	Page No.
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3.	Study Protocol (Review of literature, aim, methodology, inclusion, exclusion criteria)	✓			8-17
4.	Case Report Form (form to capture data)				
5.	Consent of Head of the PI's Department (AN2-V1/SGSOP 03/V1)	✓			18
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	for clinical trials. In other case this must be done after approval by IEC				
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26.	IEC processing fee (applicable for sponsored trials)				
27.	Any other documents				

**Please provide version no. and date of each document (for drug/device trial)*

<p>Documents submitted:</p> <p>() Complete</p> <p>() Incomplete; will submit on.....</p>
<p>Comments:</p>
<p>Receiver Name, Sign & Date: _____</p> <p>(Bioethics cell)</p> <p>Project submitted by Name & sign: Dr Uday Chand Ghoshal _____</p> <p>(Project or study team member)</p>